REMARKS

Upon entry of the amendment, claims 4, 6-9, 16-18 will be pending. Claim 16 is amended and claim 18 is added by the amendment. The amendment is only to put claim 16 in independent form. No new matter has been added by the amendment.

35 USC § 112, second paragraph

At page 2 of the Final Office Action, the U.S. Patent and Trademark Office (the PTO) rejected claims 16 and 17 as being indefinite. The PTO stated that these claims are indefinite, because they depend from claim 4, which reictes that the complementary strands of the dsRNA are non-linked. Claim 16 has been amended to be in independent form. Upon entry of the amendment, neither claims 16 or 17 will depend from claim 4. In view of the amendment, Applicants request reconsideration and withdrawal of the rejection under 35 USC § 112, second paragraph.

35 USC § 112, first paragraph (written description)

The PTO rejected claims 4 and 6-9 as failing to comply with the written description requirement. This is a new matter rejection.

The PTO stated that the claims are directed to isolated oligoribonucleotides having a double-stranded structure consisting of two separate non-linked complementary RNA strands, wherein the dsRNA is 21 nucleotides in length. The PTO also stated that the specification does not contemplate a limitation wherein the dsRNA is 21 nucleotides in length and consists of separate non-linked strands. Office Action at page 3. The PTO further stated that the claim limitation of "non-linked strands" first introduced in the amendment to the claims filed April 22, 2005, constitutes new matter." Office Action at page 3.

The rejection is respectfully traversed.

Applicants provide below two independent arguments, either of which alone shows that the claims meet the written description requirement. First, the caselaw and the PTO Written Description Guidelines provide that the written description requirement is met if, from the point

of view of one of ordinary skill in the art, the specification conveys possession of the claimed invention. The specification, plainly on its face, shows possession of 21 nucleotide dsRNAs lacking a linkage. Second, Applicants rely on In re Wertheim, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). In In re Wertheim, Applicants were permitted to use a value presented in an example as a replacement endpoint for a narrower range where a broader range had been previously claimed. The holding in In re Wertheim applies to the facts in the present case and also compels a finding that the written description requirement is met.

I

Applicants' first independent argument is as follows.

The application is directed to dsRNAs. At page 27, lines 9-27, the specification provides an example of a dsRNA 21 nucleotides in length. In that embodiment, the strands of the dsRNA are linked. Elsewhere, the specification makes it quite clear that the strands can be non-linked, as currently claimed.

The specification provides dsRNAs of several topologies, including non-linked strands, linked strands, and hairpin configurations. It is quite clear that the application conveys possession of dsRNAs having non-linked strands. For example, at page 4, line 26, of the specification, it is disclosed that "the double-stranded structure is formed by two separate RNA strands or by autocomplementary regions..." Furthermore, the application discloses that dsRNA, composed of two separate strands, can have an additional chemical linker. But to say the specification can have a linked embodiment presupposes a non-linked embodiment. This is explicitly shown in the paragraph spanning pages 4 and 5 of the application, where it is disclosed that "to inhibit dissociation in a particularly effective fashion, the cohesion of the complementary region II, which is caused by the nucleotide pairs can be increased by at least one, preferably two, further chemical linkages." Emphasis added. This language clearly refers to linkage as being permissible. Linked and non-linked are disclosed alternatives. In addition, the quoted text provides that cohesion activity can be increased.

Thus, the specification provides a linked 21 nucleotide long dsRNA and provides that the dsRNAs of the invention can be linked or non-linked. Although the current claims are not

directed literally to a range, the specification makes clear that the entire range of 15-49 nucleotide dsRNAs can be non-linked.

The case law and the PTO Written Description Guidelines provide that the review of written description must be conducted from the stand point of one ordinary skilled in the art. See MPEP 2163(II)(A)(2). It defies logic to argue that one of ordinary skill would not make the connection between the separate portions of the specification and understand that the inventors were in possession of the claimed invention.

The written description requirement is met if the specification shows that an applicant was in possession of the claimed invention at the time of filing. "When the original specification accomplishes [this], regardless of how it accomplishes it, the essential goal of the description requirement is realized." *In re Smith,* 481 F.2d 910, 914, 178 USPQ 620 (CCPA 1973). It is well accepted that "in order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *ad haec verba* support for the claimed subject matter at issue." *Purdue Pharma v. Faulding, Inc.,* 230 F.3d 1320, 56 USPQ 2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989), "the fact...that the exact words here in question...are not in the specification is not important." See also MPEP 2163.02, which provides: "The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.

Furthermore, the PTO's argument imposes an inappropriately narrow and formalistic role on one of ordinary skill in the art. In Falkner v. Inglis, 448 F.3d 1357, 1366 (CAFC May 2006), the court, relying on LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc., 424 F.3d 1336 (Fed. Cir. 2005) provided the following guidance on review from the standpoint of one of ordinary skill in the art:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because **the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor**

> **possessed the invention** and to enable such a person to make and use the invention without undue experimentation.

Emphasis added, citations omitted.

Given the disclosure of the specification and the level of skill in the art, it is clear that the specification conveys possession of the claimed invention.

For the reasons argued above, the written description requirement is satisfied. This argument is independent of and does not rely on In re Wertheim for the use of an example to construct a range or for anything else. Regardless of the Examiner's view of the In re Wertheim arguments made below, this first argument requires a finding that the claims meet the written description requirement and such a finding is requested.

II

Applicants' second independent argument is as follows.

Applicants used the working example of a 21 nucleotide dsRNA in length as a basis to amend the originally filed claims to replace the length range disclosed and claimed in the application, *i.e.*, the original length range of 15 to 49 with or without a linker. Claim 1 was amended to recite the internal value of 21 nucleotides without a linker and this is exemplified in data provided in the application.

The presence of the chemical linkage in the 21 nucleotide example does not eliminate from the scope of conception of the originally filed invention the embodiment of "linked and non-linked dsRNA." The linkage in the 21 nucleotide example is simply an exemplification of a single embodiment. Applicants have used one of the features of this embodiment, strand length of 21 nucleotides, to provide support for the amended length limitation of 21 nucleotides. There is nothing in the Example that suggests that the only way Applicants viewed that such agents could be made and used were as chemically linked molecules (as suggested by the Examiner). It is clear that the inventors contemplated that additional chemical linkages were optional elements. In the present pending claims, the pertinent feature of length, 21 nucleotides, is distinct from and separate from the other disclosed limitation, such as linked versus non-linked.

The presently pending claim length, 21 nucleotides, solves the same problem as the original range of 15-49 nucleotides, namely the drop in inhibitory effect of dsRNA in mammalian cells can be reduced using shorter dsRNA.

In response to Applicants' reliance on In re Wertheim, the PTO argued that the case provides that "[w]here it is clear, for instance, that the broad described range pertains to a different invention than the narrower (and subsumed range) then the broader range does not describe the narrower range." Office Action at page 4. The PTO, again at page 4 of the Office Action, relies on Elbashir *et al.* for the proposition that the undesirability of lengths over 30 nucleotides means that 21 nucleotide dsRNAs are different inventions and are not covered by the premise language on substitution in In re Wertheim.

The PTO's argument that Elbashir discloses that dsRNAs longer than 30 nucleotides were undesirable is irrelevant. The specification teaches the length range of 15-49 nucleotides, as well as the 21 nucleotide embodiment, and gives reasons for designing both. The specification at the paragraph spanning pages 4 and 5 states that to inhibit dissociation in a particularly effective fashion, the cohesion of the complementary regions of the dsRNA can be increased by at least one chemical linkage. As discussed above, this language clearly refers to linkage as being permissible. Linked and non-linked are disclosed alternatives.

The currently claimed unlinked dsRNAs, limited to 21 nucleotides in length, do not represent a different invention. Applicants merely limited the claims to avoid the art while still solving the same problems recognized in the specification—just as was done in In re Wertheim. A review of the specification shows that the claims as originally presented and claims as amended are directed to the problems recognized and discussed in the specification. Even if Elbashir *et al.* disclosed an additional advantage (and Applicants need not reach this question) that would not change the fact that the specification provides ample reason to regard the 21 nucleotide example as not being barred by the holding in In re Wertheim. The problems identified in the specification relate to several undesirable properties of longer dsRNAs. The undesirable properties include:

the complication and expense of preparing longer dsRNAs, see, e.g., page 1, lines 15-19, of the specification, where this problem is expressly discussed;

relatively less optimal cellular uptake, see, e.g., page 3, lines 27-29, where this problem is expressly discussed; and

non-specific effects of longer dsRNAs.

The non-specific effects of longer dsRNAs is discussed at length in the specification, see, e.g., page 3, lines 10-25:

> Surprisingly, it has emerged that an effective inhibition of the expression of the target gene can be achieved even when the complementary region I is not more than 49 base pairs in length. The procedure of providing such oligoribonucleotides is less complicated.
>
> In particular, dsRNA with a length of over 50 nucleotide pairs induces certain cellular mechanisms, for example the dsRNA dependent protein kinase or the 2-5A system, in mammalian and human cells. This leads to the disappearance of the interference effect mediated by the dsRNA which exhibits a defined sequence. As a consequence, protein biosynthesis in the cell is blocked. The present invention overcomes this disadvantage in particular.

Shorter dsRNAs, including 21 nucleotide dsRNAs that are composed of non-linked oligoribonucleotide strands, solve one or more of these problems—regardless of whether the shorter length is described as the range of 15-49, or the 21 nucleotide dsRNA of Example 2. For example, a dsRNA of 21 nucleotides, and composed of non-linked strands, like a dsRNA of 15-49 nucleotides, is less complicated to make than a longer dsRNA. Thus, the presently claimed dsRNAs of 21 nucleotides and non-linked strands solve the same problem as the original dsRNAs having 15-49 nucleotides. Even if Elbashir *et al.* encountered some additional advantage, and Applicants do not need to reach that issue, there was sufficient disclosure in the specification to show that the narrowed claims solve many of the same problems as the disclosed range.

In view of either or both of the foregoing arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 4 and 6-9 under 35 USC § 112, first paragraph, for failure to satisfy the written description requirement.

35 USC § 102

The PTO rejected claims 4 and 6-9 under 35 USC § 102(b) as being anticipated by Elbashir (2001) and under 35 USC § 102(e) as being anticipated by Tuschl *et al.* (WO 02/44321).

The PTO raised these rejections based on the incorrect priority date of July 2, 2003. As discussed above, Applicants are entitled to the priority date of PCT/DE00/00244, filed January 29, 2000. Elbashir *et al.* and Tuschl *et al.* are therefore not available as prior art, and Applicants respectfully request that the rejections under 35 USC § 102 be withdrawn.

In view of the foregoing amendments and remarks, reconsideration is respectfully requested. This application should now be in condition for allowance, and a notice to this effect is respectfully requested.

Attached is a Petition for Extension of Time for three months, and a Notice of Appeal. Please apply the $1050 fee for the Petition, the $510 fee for the Notice of Appeal, and any other necessary charges, or any credits, to Deposit Account No. 50/2762, referencing Attorney Docket No. A2038-704820.

Respectfully submitted,

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